Remarks

Claims 34 and 51 have been amended to address informalities. Claim 34 has been rewritten to recite an "animal model" in the last phrase of step e), consistent with the recitation of "animal model" earlier in that step. Claim 51 has been rewritten to recite an "$\alpha_3\beta_3\gamma_2$ $GABA_A$ subtype receptor" in the last phrase of step c), as described in the specification as filed at page 33, line 6, to page 38, line 3. No new matter is added by these amendments. With these amendments, the claims pending are claims 24-35 and 51-55.

The Examiner made the Action mailed April 19, 2005 final, asserting that "Applicant's amendment necessitated the new ground(s) of rejection" presented therein. Claims 24-35 originally recited the $\alpha_2\beta_3\gamma_2$ and $\alpha_3\beta_3\gamma_2$ subunits in the alternative. In the response dated January 13, 2005, Applicants rewrote these claims to recite only the $\alpha_3\beta_3\gamma_2$ subunit. The Examiner cited a new reference (Ladduwahetty et al., U.S. Patent 6,444,666) and relied upon it to finally reject the claims in the Office Action dated April 19, 2005.

Applicants respectfully submit that this action was made final prematurely. "A second or any subsequent action on the merits in any application . . . should not be made final if it

includes a rejection, on prior art not of record, of any claim amended to include limitations which should reasonably have been expected to be claimed." M.P.E.P. 706.07(a). Because the rejections in the Office Action dated September 13, 2004 were based only upon the $\alpha_2\beta_3\gamma_2$ subunit, the Examiner should reasonably have expected the Applicants to amend the claims to recite only the $\alpha_3\beta_3\gamma_2$ subunit. As such, the Office Action including the rejection based on U.S. 6,444,666 should not have been made final.

Applicants therefore respectfully request that the Examiner withdraw the finality of the Office Action dated April 19, 2005.

Claims 24-35 and 51-55 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,444,666 (Ladduwahetty et al.) in view of H. Mohler et al., "Heterogeneity of $GABA_A$-Receptors: Cell Specific Expression, Pharmacology, and Regulation," 20 Neurochemical Res., 631-36 (1995) (Mohler et al.). Ladduwahetty et al. is directed to a class of triazolopyridazine compounds that have high binding affinity for the α_2 and/or α_3 subunits, and describes an assay method for use in determining the binding affinities (K_i) of the compounds. Mohler et al. describes some of the different $GABA_A$-receptor subtypes and their respective pharmacologies.

The combination of Ladduwahetty et al. and Mohler et al. does not render claims 24-35 and 51-55 obvious. These claims recite screening methods in which *in vitro* efficacy and EC_{50} values are measured and compared in order to identify compounds having anxiolytic activity. As described in the application as filed, EC_{50} values do not necessarily correlate with binding affinities or efficacies (page 8, lines 1-15), and the claimed methods may be performed without measuring binding affinities (page 7, lines 12-14). In contrast, Ladduwahetty et al. identifies its compounds as having high binding affinities K_i (e.g., col. 2, lines 20-26; col. 3, lines 4-18), and describes a screening method based only on binding affinity (col. 16, line 23 - col. 17, line 10). Binding affinity has been the basis for conventional screening methods for receptor-selective compounds. See Paul J. Whiting, "The $GABA_A$ receptor gene family: New opportunities for drug development," 6 Current Opinion in Drug Discovery & Development, 648-57, 652 (2003) (copy provided with this paper) ("The traditional approach to develop compounds that are selective for, for example, a receptor subtype, is to aim for binding affinity or selectivity, which can be achieved through the use of conventional radioligand binding assays.") The skilled artisan reading Ladduwahetty et al. would be taught that binding affinity is the important parameter, and conduct conventional screening assays based on binding affinity, not on

efficacy and EC_{50} values. Mohler et al. provides no additional teachings with respect to screening methods. Moreover, the Whiting reference at page 652 indicates that a screen based on binding selectivity would miss some compounds that are functionally selective, and would identify compounds that are not functionally selective. Clearly, the Ladduwahetty and Mohler references do not render the claimed invention obvious.

Applicants respectfully request reconsideration and withdrawal of the rejection of claims 24-35 and 51-55 made under 35 U.S.C. § 103(a).

Applicants urge the Examiner to contact the Applicants' undersigned representative at (312) 913-0001 if he believes that a discussion would expedite prosecution of this application.

Respectfully submitted,

Dated: June 20, 2005 By: _____

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